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Bireociclib plus Fulvestrant in the second line treatment for HR+/HER2− Advanced or Metastatic Breast Cancer: A Cost-Effectiveness Analysis

Yuanbao Xie[1] , Yu Chen[1] , Xinyue Yuan[1] , Jingjing Wu[1] , Fei Liu[2] , Xianghui Duan[2] , Ming Hu[1#]

1.West China School of Pharmacy , Sichuan University , Chengdu610225 , China
2.Clinical Science Department, Xuanzhu Biopharmaceutical Co.Ltd., Beijing100061, China.

Background & Objectives

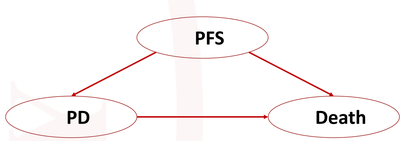
Breast cancer remains a major global health burden and the most common cause of cancer-related death among women worldwide. Hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2−) disease represents the predominant breast cancer subtype, accounting for approximately 60–70% of all cases. Although survival outcomes for early-stage breast cancer have improved substantially, prognosis remains poor for patients with advanced or metastatic breast cancer (ABC/MBC), highlighting the urgent need for effective long-term treatment strategies.Cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors combined with endocrine therapy have transformed the treatment landscape for HR+/HER2− ABC and are recommended by current clinical guidelines as standard second-line therapy after endocrine progression.

Abemaciclib is widely used in clinical practice with established efficacy. Recently, Bireociclib, a novel highly selective CDK4/6 inhibitor approved in China, demonstrated promising efficacy and improved tolerability in the phase III BRIGHT-2 trial.Despite significant clinical benefits, prolonged use of CDK4/6 inhibitors is associated with substantial economic burden.

Therefore, this study aimed to evaluate the cost-effectiveness of Bireociclib plus fulvestrant versus Abemaciclib plus fulvestrant for HR+/HER2− ABC from the perspective of the Chinese healthcare system.

Methods

- **Study Design**



A partitioned survival model (PSM) with three health states (PFS, PD, and death) was developed from the perspective of the Chinese healthcare system. The model adopted a 15-year time horizon, 28-day cycle length, and 5% annual discount rate. Cost-effectiveness was evaluated using ICERs with a WTP threshold of 95,749 CNY/QALY.

- **Clinical Data and MAIC**

Clinical efficacy and safety data were obtained from the BRIGHT-2 and MONARCH-2 phase III trials. In the absence of head-to-head evidence, MAIC was conducted to adjust for cross-trial baseline heterogeneity. Adjusted HRs for PFS and OS were derived from weighted BRIGHT-2 IPD.

- **Survival Extrapolation**

Pseudo-IPD were reconstructed from published Kaplan–Meier curves using the Guyot algorithm. Standard parametric and spline models were evaluated, with best-fit models selected based on AIC/BIC and clinical plausibility.

Two extrapolation scenarios were explored:

Scenario 1(Priamry): Independent fitting using identical model structures for both treatment arms

Scenario 2: HR-based extrapolation assuming proportional treatment effects

- **Cost and Utility Inputs**

Direct medical costs included drug acquisition, follow-up, disease management, subsequent treatment, and AE management costs. Health utilities for PF and PD states were derived from published literature.

- **Sensitivity Analyses**

One-way sensitivity analysis, probabilistic sensitivity analysis (PSA), and scenario analyses were performed to evaluate model uncertainty and robustness.

Results

(1) Survival Extrapolation

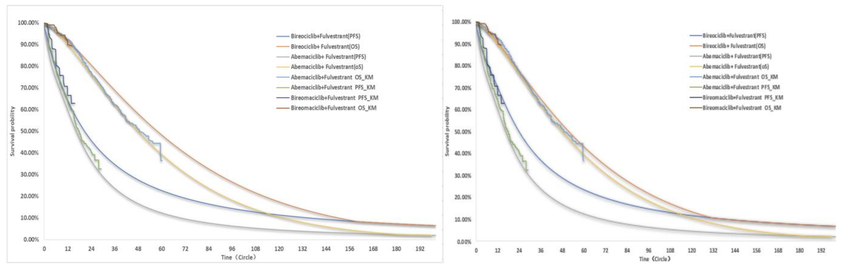


Figure 1 Survival Extrapolation(Left:scenario 1 ;Right:scenario 2)

Scenario 1 used independent parametric survival fitting for both treatment arms, with spline (k=2, log-odds) selected for PFS and Gamma selected for OS. Scenario 2 applied HR-based extrapolation using MAIC-adjusted HRs, with Bireociclib plus fulvestrant demonstrating improved OS (HR=0.885) and PFS (HR=0.701) versus Abemaciclib plus fulvestrant.

(2)Base-case Analysis

Table 2 Outcomes of the primary scenario

Outcome	Bireociclib + fulvestrant	Abemaciclib + fulvestrant
Total Cost (CNY)	340,657	342,858
Total QALYs	3.073	2.487
Incremental cost	-2200	
Incremental QALYs	0.585	
ICER (CNY/QALY)	-3,758	
Conclusion	Dominant	

Compared with Abemaciclib plus fulvestrant, Bireociclib plus fulvestrant resulted in lower total costs and improved health outcomes under the promary extrapolation scenarios.

(3) Sensitivity Analysis

One-way sensitivity analysis showed that the model results were primarily driven by best supportive care costs and drug acquisition costs in both treatment arms. Chemotherapy costs and costs associated with subsequent CDK4/6 inhibitor plus endocrine therapy had moderate effects on the ICER, whereas laboratory test costs and end-of-life care costs had relatively limited influence on model outcomes. Overall, the base-case conclusions remained robust across all parameter variations.

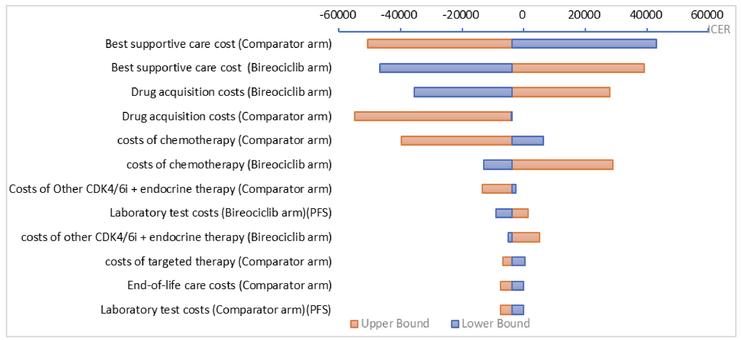


Figure 1 Tornado Diagram for One-way Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) demonstrated that most simulations were distributed below the willingness-to-pay (WTP) threshold line, indicating favorable cost-effectiveness of Bireociclib plus fulvestrant compared with Abemaciclib plus fulvestrant. At the predefined WTP threshold of 95,749 CNY/QALY, the probability of Bireociclib plus fulvestrant being cost-effective was 84.60%, supporting the robustness of the base-case results under parameter uncertainty

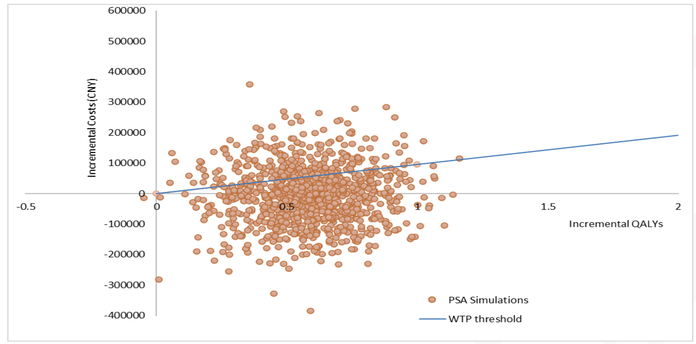


Figure 2 Probabilistic Sensitivity Analysis (PSA) Scatter Plot

(4) Scenario Analysis

Table 3 Outcomes of the scenario 2

Incremental cost	-41,776
Incremental QALYs	0.479
ICER (CNY/QALY)	-87,299
Conclusion	Dominant

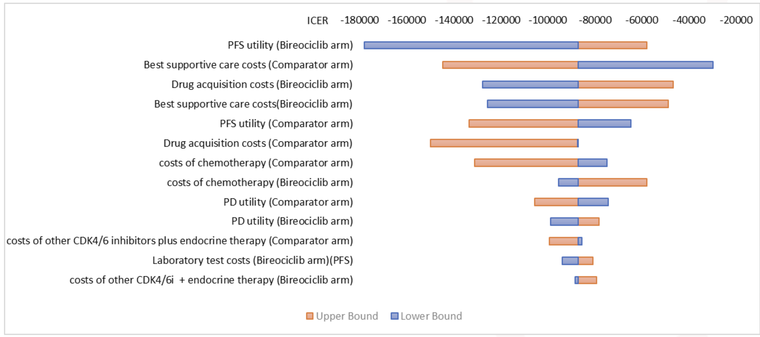


Figure 3 Tornado Diagram for One-way Sensitivity Analysis of the scenario 2

Scenario 2 results were generally consistent with the base-case analysis. PFS utility, best supportive care costs, and drug acquisition costs were the main drivers of uncertainty. Across all parameter variations, Bireociclib plus fulvestrant remained cost-effective compared with Abemaciclib plus fulvestrant.

Conclusion

Current evidence suggests that bireociclib combined with fulvestrant is a cost-effective alternative to abemaciclib plus fulvestrant. However, given the limited 8-month follow-up of BRIGHT-2 trial, these findings warrant further as more mature long-term survival data become available

First Author:Yuanbao Xie email:x294650@163.com ; #corresponding author:huming@scu.edu.cn